WHAT IS CLAIMED IS:

1. A compound of Formula I:

$$(R^{4})_{n}$$
 R^{3}
 R^{1}
 R^{10}
 R^{13}
 R^{2}
 R^{0x}
 R^{14}

5 or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

a is 0 or 1; b is 0 or 1;

10 b is 0 or 1; m is 0, 1, or 2;

n is 0, 1, 2 or 3;

r is 0 or 1;

s is 0 or 1;

15 t is 0, 1 or 2;

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u is 0, 1, or 2;

R1 and R2 are independently selected from: H, (C1-C6)alkyl, aryl, heterocyclyl and (C3-C6)cycloalkyl, optionally substituted with one, two or three substituents selected from R7;

R³ is selected from:

- 1) Hydrogen,
- 2) C₁-C₁₀ alkyl;
- 3) C_1 - C_{10} alkyl-O- R_0 ,
- 4) C2-C10 alkenyl-O-Rd,
- 5 C2-C10 alkynyl-O-Rd,
 - 6) (C1-C6-alkylene)_nC3-C8 cycloalkyl-O-Rd,
 - 7) C_1 - C_{10} alkyl- $(C=O)_b$ - NR^cR^c ,
 - 8) C2-C10 alkenyl-(C=O)bNRcRc',
 - 9) C2-C10 alkynyl-(C=O)bNRcRc',
- 10 (C₁-C₆-alkylene)_nC₃-C₈ cycloalkyl-(C=O)_bNR^cR^c',
 - 11) C_1 - C_{10} alkyl- $S(O)_m$ -Rd,
 - 12) C_2 - C_{10} alkenyl- $S(O)_m$ - R_d ,
 - 13) C_2 - C_{10} alkynyl- $S(O)_m$ -Rd,
 - 14) (C₁-C₆-alkylene)_nC₃-C₈ cycloalkyl- S(O)_m-Rd,
- said alkyl, alkenyl, alkynyl and cycloalkyl are optionally substituted with one or more substituents selected from R⁶;

R⁴ is independently selected from:

- 1) $(C=O)_aO_bC_1-C_{10}$ alkyl,
- 20 2) $(C=O)_aO_baryl$,
 - 3) CO₂H,
 - 4) halo,
 - 5) CN,
 - 6) OH,

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- 7) ObC1-C6 perfluoroalkyl,
 - 8) $O_a(C=O)_bNRSR9$,
- 9) $S(O)_m R^a$,
- 10) $S(O)_2NR^8R^9$,
- 11) $-OPO(OH)_2$;
- said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R⁷;

R⁵ is selected from:

- 1) hydrogen;
- 35 2) $(C=O)_aO_bC_1-C_{10}$ alkyl,

- 3) $(C=O)_aO_baryl$,
- 4) CO₂H,
- 5) halo,
- 6) CN,
- 5 7) OH,
 - 8) ObC1-C6 perfluoroalkyl,
 - 9) $O_a(C=O)_bNR^8R^9$,
 - 10) $S(O)_mR^a$,
 - 11) $S(O)_2NR^8R^9$,
- 10 12) -OPO(OH)₂;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R⁷;

R6 is independently selected from:

- 15 1) $(C=O)_aO_bC_1-C_{10}$ alkyl,
 - 2) $(C=O)_aO_baryl$,
 - 3) C2-C₁₀ alkenyl,
 - 4) C2-C₁₀ alkynyl,
 - 5) (C=O)_aO_b heterocyclyl,
- 20 6) CO₂H,
 - 7) halo,
 - 8) CN,
 - 9) OH,
 - 10) ObC1-C6 perfluoroalkyl.
- 25 11) $O_a(C=O)_bNR^8R^9$,
 - 12) $S(O)_mRa$,
 - 13) $S(O)_2NR^8R^9$,
 - 14) oxo,
 - 15) CHO,
- 30 16) $(N=O)R^8R^9$, or
 - 17) (C=O)_aO_bC₃-C₈ cycloalkyl,
 - 18) $-OPO(OH)_2$;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R7;

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R⁷ is selected from:

- 1) $(C=O)_rO_s(C_1-C_{10})$ alkyl,
- 2) $O_r(C_1-C_3)$ perfluoroalkyl,
- 3) oxo,
- 5 4) OH,
 - 5) halo,
 - 6) CN.
 - 7) (C2-C10)alkenyl,
 - 8) (C2-C10)alkynyl,
- 10 9) $(C=O)_rO_s(C_3-C_6)$ cycloalkyl,
 - 10) $(C=O)_rO_s(C_0-C_6)$ alkylene-aryl,
 - 11) $(C=O)_rO_s(C_0-C_6)$ alkylene-heterocyclyl,
 - 12) $(C=O)_rO_s(C_0-C_6)$ alkylene- $N(R^b)_2$,
 - 13) $C(O)R^a$,
- 15 (C0-C6)alkylene-CO₂R^a.
 - 15) C(O)H,
 - 16) (C₀-C₆)alkylene-CO₂H,
 - 17) $(C=O)_rN(R^b)_2$,
 - 18) $S(O)_mR^a$,
- 20 19) $S(O)_2N(R^b)_2$, and
 - $-OPO(OH)_2$;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from Rb, OH, (C1-C6)alkoxy, halogen, CO2H, CN,

O(C=O)C1-C6 alkyl, oxo, NO2 and N(Rb)2;

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R8 and R9 are independently selected from:

- 1) H,
- 2) $(C=O)O_bC_1-C_{10}$ alkyl,
- 3) (C=O)ObC3-C8 cycloalkyl,
- 30 4) (C=O)Obaryl,
 - 5) (C=O)Obheterocyclyl,
 - 6) C₁-C₁₀ alkyl,
 - 7) aryl,
 - 8) C2-C10 alkenyl,
- 35 9) C₂-C₁₀ alkynyl,

- 10) heterocyclyl,
- 11) C3-C8 cycloalkyl,
- 12) SO₂Ra, and
- 13) $(C=O)NRb_2$,
- said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from R7, or

R8 and R9 can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R7;

R10 is selected from: H and F:

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R11 and R12 are independently selected from: F and -CH2F;

 R^{13} and R^{14} are independently selected from: H and -CH₂F;

20 R^{ox} is absent or is oxo:

R^a is independently selected from: (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl, optionally substituted with one, two or three substituents selected from R⁷;

- Rb is independently selected from: H, (C1-C6)alkyl, aryl, heterocyclyl, (C3-C6)cycloalkyl, (C=O)OC1-C6 alkyl, (C=O)C1-C6 alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NReRe 'or S(O)2Ra, optionally substituted with one, two or three substituents selected from R⁷;
- R^cand R^c are independently selected from: H, (C₁-C₆)alkyl, aryl, NH₂, OH, OR^a, -(C₁-C₆)alkyl-OH, -(C₁-C₆)alkyl-O-(C₁-C₆)alkyl, (C=O)OC₁-C₆ alkyl, (C=O)C₁-C₆ alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NR^eR^e, S(O)₂R^a and -(C₁-C₆)alkyl-N(R^b)₂, wherein the alkyl is optionally substituted with one, two or three substituents selected from R⁷; or
 - R^c and R^c' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in

addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷;

- Rd is selected from: H, (C1-C6)alkyl, -(C2-C6)alkyl-OH, -(C1-C6)alkyl-O-(C1-C6)alkyl and (C1-C6)alkyl-N(R^b)2, wherein the alkyl is optionally substituted with one, two or three substituents selected from R⁷;
- Re and Re' are independently selected from: H, (C1-C6)alkyl, aryl, heterocyclyl and (C3-C6)cycloalkyl, optionally substituted with one, two or three substituents selected from R⁷; or

Re and Re' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷

2. The compound according to Claim 1 of Formula II:

$$(R^{4})_{n}$$

$$R^{1}$$

$$R^{1}$$

$$R^{13}$$

$$R^{2}$$

$$R^{0x}$$

$$R^{14}$$

$$R^{14}$$

$$R^{18}$$

$$R^{14}$$

$$R^{19}$$

$$R^{19}$$

$$R^{19}$$

$$R^{19}$$

$$R^{11}$$

or a pharmaceutically acceptable salt or stereoisomer thereof,

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wherein:

```
a is
              0 or 1;
      b is
              0 or 1;
 5
      m is
              0, 1, or 2;
              0, 1, 2 or 3;
      n is
      r is
              0 or 1;
      s is
              0 or 1;
              0 or 1;
      t is
10
              0 or 1;
      u is
```

 R^1 and R^2 are independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl and (C₃-C₆)cycloalkyl, optionally substituted with one, two or three substituents selected from R^7 ;

15 R³ is selected from:

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- 1) hydrogen;
- 2) C_1 - C_{10} alkyl;
- 3) C_1 - C_{10} alkyl-O- R^d ,
- 4) C2-C₁₀ alkenyl-O-Rd,
- 20 5) C2-C10 alkynyl-O-Rd,
 - 6) (C₁-C₆-alkylene)_nC₃-C₈ cycloalkyl-O-Rd,
 - 7) C_1-C_{10} alkyl- $(C=O)_b-NR^cR^c$,
 - S) C_2 - C_{10} alkenyl- $(C=O)_bNR^cR^c$,
 - 9) C2-C₁₀ alkynyl-(C=O)_bNRcRc'.
 - 10) (C₁-C₆-alkylene)_nC₃-C₈ cycloalkyl-(C=O)_bNR^cR^c,
 - 11) C_1 - C_{10} alkyl- $S(O)_m$ - R^d ,
 - 12) C2-C10 alkenyl- S(O)_m-Rd,
 - 13) C_2 - C_{10} alkynyl- $S(O)_m$ -Rd,
 - 14) (C1-C6-alkylene)_nC3-C8 cycloalkyl- S(O)_m-Rd,

said alkyl, alkenyl, alkynyl and cycloalkyl are optionally substituted with one or more substituents selected from R⁶;

R⁴ is independently selected from:

35 1) $(C=O)_aO_bC_1-C_{10}$ alkyl,

- 2) $(C=O)_aO_baryl$,
- 3) CO₂H,
- 4) halo,
- 5) CN,
- 5 6) OH,
 - 7) ObC1-C6 perfluoroalkyl,
 - 8) $O_a(C=O)_bNR^8R^9$,
 - 9) $S(O)_mR^a$,
 - 10) $S(O)_2NR^8R^9$, and
- 10 11) -OPO(OH)₂;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R⁷;

R⁵ is selected from:

- 15 1) hydrogen;
 - 2) $(C=O)_aO_bC_1-C_{10}$ alkyl,
 - 3) $(C=O)_aO_baryl$,
 - 4) CO₂H,
 - 5) halo,
- 20 6) CN,
 - 7) OH,
 - 8) ObC1-C6 perfluoroalkyl,
 - 9) $O_a(C=O)_bNR^8R^9$,
 - 10) $S(O)_m R^a$,
- 25 11) $S(O)_2NR^8R^9$,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R⁷;

. . . .

R6 is independently selected from:

- 30 1) $(C=O)_aO_bC_1-C_{10}$ alkyl,
 - 2) $(C=O)_aO_baryl$,
 - 3) C2-C10 alkenyl,
 - 4) C2-C₁₀ alkynyl,
 - 5) (C=O)aOb heterocyclyl,
- 35 6) CO₂H,

7) halo, 8) CN, 9) OH. ObC1-C6 perfluoroalkyl, 10) $O_a(C=O)_bNR^8R^9$, 5 11) S(O)_mRa, 12) $S(O)_2NR^8R^9$, 13) 14) oxo, 15) CHO, $(N=O)R^8R^9$, or 10 16) 17) (C=O)aObC3-C8 cycloalkyl, and 18) $-OPO(OH)_2$; said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R7; 15 R⁷ is selected from: 1) $(C=O)_rO_s(C_1-C_{10})$ alkyl, 2) O_r(C₁-C₃)perfluoroalkyl, 3) oxo, 20 4) OH, 5) halo, 6) CN, 7) (C2-C10)alkenyl, (C2-C10)alkynyl, 8) 25 9) $(C=O)_rO_s(C_3-C_6)$ cycloalkyl, 10) $(C=O)_rO_s(C_0-C_6)$ alkylene-aryl, $(C=O)_rO_s(C_0-C_6)$ alkylene-heterocyclyl, 11) 12) (C=O)_rO_s(C₀-C₆)alkylene-N(R^b)₂, $C(O)R^{a}$ 13) 30 14) (C0-C6)alkylene-CO2Ra 15) C(O)H, (C0-C6)alkylene-CO2H, 16) $C(O)N(R^b)_2$, 17) $S(O)_m R^a$, 18)

 $S(O)_2N(R^b)_2$; and

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19)

20) $-OPO(OH)_2$;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from Rb, OH, (C1-C6)alkoxy, halogen, CO2H, CN, O(C=O)C1-C6 alkyl, oxo, NO2 and N(Rb)2;

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R8 and R9 are independently selected from:

- 1) H,
- 2) $(C=O)O_bC_1-C_{10}$ alkyl,
- 3) (C=O)O_bC₃-C₈ cycloalkyl,
- 10 4) (C=O)Obaryl,
 - 5) (C=O)Obheterocyclyl,
 - 6) C_1 - C_{10} alkyl,
 - 7) aryl.
 - 8) C2-C₁₀ alkenyl,
- 15 9) C2-C₁₀ alkynyl,
 - 10) heterocyclyl,
 - 11) C3-C8 cycloalkyl,
 - 12) SO₂Ra, and
 - 13) $(C=O)NRb_2$,

said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from R⁷, or

R⁸ and R⁹ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷:

R¹¹ and R¹² are independently selected from: F and -CH₂F;

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 R^{13} and R^{14} are independently selected from: H and -CH₂F, provided that when t is 1, R^{14} is H; and when u is 1, R^{13} is H;

R^{ox} is absent or is oxo;

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R^a is independently selected from: (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl, optionally substituted with one, two or three substituents selected from R⁷;

Rb is independently selected from: H, (C1-C6)alkyl, aryl, heterocyclyl, (C3-C6)cycloalkyl, (C=O)OC1-C6 alkyl, (C=O)C1-C6 alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NRee or S(O)2Ra, optionally substituted with one, two or three substituents selected from R7;

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- R^cand R^c are independently selected from: H, (C₁-C₆)alkyl, aryl, NH₂, OH, OR^a, -(C₁-C₆)alkyl-OH, -(C₁-C₆)alkyl-O-(C₁-C₆)alkyl, (C=O)OC₁-C₆ alkyl, (C=O)C₁-C₆ alkyl, (C=O)Aryl, (
- R^c and R^c' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷;
- Rd is selected from: H, (C1-C6)alkyl, -(C2-C6)alkyl-OH, -(C1-C6)alkyl-O-(C1-C6)alkyl and (C1-C6)alkyl-N(R^b)2, wherein the alkyl is optionally substituted with one, two or three substituents selected from R⁷;
 - Re and Re' are independently selected from: H, (C1-C6)alkyl, aryl, heterocyclyl and (C3-C6)cycloalkyl, optionally substituted with one, two or three substituents selected from R⁷; or
 - Re and Re' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R7.
 - 3. The compound according to Claim 2 of the Formula III:

or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

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a is 0 or 1;

b is 0 or 1;

m is 0, 1, or 2;

n is 0, 1 or 2;

10 r is 0 or 1;

s is 0 or 1;

t is 0 or 1;

R¹ and R² are independently selected from: H, (C₁-C₆)alkyl, aryl and (C₃-C₆)cycloalkyl, optionally substituted with one, two or three substituents selected from R⁷;

R⁴ is independently selected from:

- 4) halo,
- 5) OH,
- 20 6) ObC1-C6 perfluoroalkyl,

R⁵ is selected from:

- 1) hydrogen,
- 2) halo,
- 3) OH,
- 4) ObC1-C6 perfluoroalkyl,

5

R⁷ is selected from:

- 1) $(C=O)_rO_s(C_1-C_{10})$ alkyl,
- 2) $O_r(C_1-C_3)$ perfluoroalkyl,
- 3) oxo,
- 10 4) OH,
 - 5) halo,
 - 6) CN,
 - 7) (C2-C10)alkenyl,
 - 8) (C_2-C_{10}) alkynyl,
- 15 9) $(C=O)_rO_s(C_3-C_6)$ cycloalkyl,
 - 10) $(C=O)_rO_s(C_0-C_6)$ alkylene-aryl,
 - (C=O) $_{r}O_{s}(C_{0}-C_{6})$ alkylene-heterocyclyl,
 - 12) $(C=O)_rO_s(C_0-C_6)$ alkylene- $N(Rb)_2$,
 - 13) $C(O)R^{a}$,
- 20 (C₀-C₆)alkylene-CO₂R^a,
 - 15) C(O)H,
 - 16) (C₀-C₆)alkylene-CO₂H, and
 - 17) $C(O)N(R^b)_2$,
 - 18) $S(O)_mR^a$, and
- 25 19) $S(O)_2N(R^b)_2$;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b, OH, (C₁-C₆)alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, NO₂ and N(R^b)₂;

- 30 R8 and R9 are independently selected from:
 - 1) H,
 - 2) $(C=O)O_bC_1-C_{10}$ alkyl,
 - 3) (C=O)ObC3-C8 cycloalkyl,
 - 4) (C=O)Obaryl,
- 35 (C=O)Obheterocyclyl,

- 6) C₁-C₁₀ alkyl,
- 7) aryl,

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- 8) C2-C10 alkenyl,
- 9) C2-C₁₀ alkynyl,
- 10) heterocyclyl,
- 11) C3-C8 cycloalkyl,
- 12) SO₂Ra, and
- 13) $(C=O)NRb_2$,

said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from R7, or

 R^8 and R^9 can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R^7 ;

R12 is selected from: F and -CH₂F;

20 R¹⁴ is selected from: H and -CH₂F, provided that when t is 1, R¹⁴ is H;

R^a is independently selected from: (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl, optionally substituted with one, two or three substituents selected from R⁷;

Rb is independently selected from: H, (C1-C6)alkyl, aryl, heterocyclyl, (C3-C6)cycloalkyl, (C=O)OC1-C6 alkyl, (C=O)C1-C6 alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NReRe 'or S(O)2Ra, optionally substituted with one, two or three substituents selected from R⁷;

R^cand R^c ' are independently selected from: H, (C₁-C₆)alkyl, aryl, NH₂, OH, OR^a, -(C₁-C₆)alkyl-OH, -(C₁-C₆)alkyl-O-(C₁-C₆)alkyl, (C=O)OC₁-C₆ alkyl, (C=O)C₁-C₆ alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NR^eR^e ', S(O)₂R^a and -(C₁-C₆)alkyl-N(R^b)₂, wherein the alkyl is optionally substituted with one, two or three substituents selected from R⁷; or

Rc and Rc' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in

addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R7;

Re and Re' are independently selected from: H, (C1-C6)alkyl, aryl, heterocyclyl and (C3-C6)cycloalkyl, optionally substituted with one, two or three substituents selected from R⁷; or

Re and Re' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R7.

4. The compound according to Claim 3 of the Formula IV:

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or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

20 a is 0 or 1; b is 0 or 1; m is 0, 1, or 2; r is 0 or 1;

s is 0 or 1;

R¹ and R² are independently selected from: H and (C₁-C₆)alkyl, optionally substituted with one, two or three substituents selected from R⁷;

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R⁴ is independently selected from:

- 1) halo,
- 2) OH,
- 3) ObC1-C6 perfluoroalkyl,

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R7 is selected from:

- 1) $(C=O)_rO_s(C_1-C_{10})$ alkyl,
- 2) $O_r(C_1-C_3)$ perfluoroalkyl,
- 3) oxo,
- 15 4) OH,
 - 5) halo,
 - 6) CN,
 - 7) (C2-C10)alkenyl,
 - 8) (C_2-C_{10}) alkynyl,
- 20 9) $(C=O)_{r}O_{s}(C_{3}-C_{6})$ cycloalkyl,
 - 10) $(C=O)_rO_s(C_0-C_6)$ alkylene-aryl,
 - 11) $(C=O)_rO_s(C_0-C_6)$ alkylene-heterocyclyl,
 - 12) $(C=O)_rO_s(C_0-C_6)$ alkylene- $N(R^b)_2$,
 - 13) $C(O)R^a$,
- 25 (C₀-C₆)alkylene-CO₂R^a
 - 15) C(O)H,
 - 16) (C₀-C₆)alkylene-CO₂H, and
 - 17) $C(O)N(R^b)_2$,
 - 18) $S(O)_mR^a$, and
- 30 19) $S(O)_2N(R^b)_2$;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b, OH, (C₁-C₆)alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, NO₂ and N(R^b)₂;

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R8 and R9 are independently selected from:

- 1) H,
- 2) $(C=O)O_bC_1-C_{10}$ alkyl,
- 3) (C=O)ObC3-C8 cycloalkyl,
- 4) (C=O)Obaryl,
- 5) (C=O)Obheterocyclyl,
 - 6) C₁-C₁₀ alkyl,
 - 7) aryl,
 - 8) C2-C10 alkenyl,
 - 9) C2-C₁₀ alkynyl,
- 10 10) heterocyclyl,

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- 11) C3-C8 cycloalkyl,
- 12) SO₂Ra, and
- 13) $(C=O)NRb_2$,

said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from R⁷, or

R⁸ and R⁹ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷;

R^a is independently selected from: (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl, optionally substituted with one, two or three substituents selected from R⁷;

 R^b is independently selected from: H, (C1-C6)alkyl, aryl, heterocyclyl, (C3-C6)cycloalkyl, (C=O)OC1-C6 alkyl, (C=O)C1-C6 alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NReRe 'or $S(O)_2R^a$, optionally substituted with one, two or three substituents selected from R^7 ;

Rcand Rc are independently selected from: H, (C1-C6)alkyl, aryl, NH2, OH, ORa, -(C1-C6)alkyl-OH, -(C1-C6)alkyl-O-(C1-C6)alkyl, (C=O)OC1-C6 alkyl, (C=O)C1-C6 alkyl, (C=O)aryl, (C=O)heterocyclyl, (C=O)NReRe, S(O)₂Ra and -(C1-C6)alkyl-N(Rb)₂, wherein the alkyl is optionally substituted with one, two or three substituents selected from R7; or

R° and R° can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R⁷;

Re and Re' are independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl and (C₃-C₆)cycloalkyl, optionally substituted with one, two or three substituents selected from R⁷; or

- 10 Re and Re' can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R7.
 - 5. A compound selected from:

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- (2S)-4-(2,5-difluorophenyl)-N-[(4R,6S)-6-fluoro-1-methylazepan-4-yl]-2-(hydroxymethyl)-N-methyl-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxamide
- 20 (2S)-4-(2,5-difluorophenyl)-N-[(4S,6R)-6-fluoro-1-methylazepan-4-yl]-2-(hydroxymethyl)-N-methyl-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxamide

or a pharmaceutically acceptable salt thereof.

25 6. The compound according to Claim 1 which is selected from:

R ₄ F R ₅
N R ₂
F
N-N-R ₁

R ₁	R ₂	R ₃	R_4	R ₅
^	CH₂OH	Me	F	Н
~~	CH₂OH	Me	F	н
	CH₂OH	Me	F	н
N	CH₂OH	Me	F	Н
N	CH ₂ OH	Me	F	 H
N	CH ₂ OH	Me	F	н
N	CH₂OH	Me	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
N N	CH ₂ OH	Me	F	н
N N	CH ₂ OH	Ме	F	н
	СН₂ОН	Me	F	Н
NNNNH	CH₂OH	Me	F	н
N-N	CH₂OH	Me	F	н
\(\bigc\)	CH ₂ OH	Ме	F	н
ON	CH₂OH	Me	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
S N	CH₂OH	Me	F	н
N	CH₂OH	Me	F	н
ON ON	^{∕le} CH₂OH	Me	F	н
N	CH ₂ OH	Me	·F	н
N O	CH₂OH Me	Me	F	н
Me	Me	Me	F	Н
Me		Me	F	н
Me	ОН	Me	F	Н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	NH ₂	Me	F	Н
Me	∕ ОН	Me	F	н
Me	NH ₂	Me	F	н
Me	Ph NH ₂	Me	F	н
Me	OH	Me	F	н
Me	\sim NH ₂	Me	F	Н
Me	NH ₂	Me	F	н
Me	NH ₂ CHF ₂	Me	F	Н
Me	CHF ₂ NH ₂	Me	F	н
Me	NH ₂ CHF ₂	Me	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	~~~N	Me	F	н
Me	N	Me	F	н
Me	~~~NH	Me	F	н
Me	NOMe	Me	F	н
Me	$N \rightarrow NH_2$	Me	F	Н
Me	\sim	Me	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	N, N	Me	F	н
Me	No	Me	F	н
Me	N N N N N N N N N N N N N N N N N N N	Me	F	н
Me	√√N ^S	Me	F	н
Me	CH₂OH		F	н
Me	CH₂OH	/	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	CH₂OH		F	н
Me	CH₂OH	\nearrow	F	Н
Me	CH₂OH		F	Н
Me	CH₂OH		F	Н
Me	CH₂OH	\square	F	Н
Me	CH ₂ OH	CN	F	Н
Me	CH ₂ OH		F	Н
Me	CH₂OH	\wedge	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	CH₂OH	Мө	CI	н
Me	СН₂ОН	Me	Br	н
Ме	CH₂OH	Me	CN	н
Me	CH₂OH	Me	Me	H
Me	CH ₂ OH	Ме	CF ₃	н
Me	СН₂ОН	Me	NO ₂	н
Me	CH₂OH	Me	F	ОН
Me	CH₂OH	Me	F	NH ₂
Me	CH₂OH	Me	F	F
Me	CH ₂ OH	Me - 146 -	F	SH

	R ₄ R ₃ N R ₁	F R ₅		
R ₁	R ₂	R ₃	R ₄	R ₅
	CH ₂ OH	Me	F	Н
~	CH₂OH	Me	F	Н
	CH₂OH	Me	F	н
N	CH₂OH	Me	F	н
N	CH₂OH	 Me	F	н
N	СН₂ОН	Me	F	н
N	CH₂OH	Me	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
N N	CH₂OH	Me	F	н
N N	CH₂OH	Ме	F	Н
	CH₂OH	Ме	F	н
N N NH	CH₂OH	Ме	F	н
N-N	CH₂OH	Ме	F	Н
O	CH₂OH	Me	F	н
O _N	CH ₂ OH	Me	F	 Н

R ₁	R ₂	R ₃	R ₄	R ₅
S	CH₂OH	Me	F	Н
	CH₂OH	Me	F	н
OMe	CH₂OH	Ме	F	н
N	CH ₂ OH	Me	F	н
OMe	CH₂OH	Me	F	Н
Me	Ме	Me	F	.
Me		Me	F	н
Ме	∕OH	Me	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	NH ₂	Me	F	н
Me	ОН	Me	F	н
Me	\sim NH ₂	Me	F	н
Me	Ph NH ₂	Me	F	Н
Me	OH	Me	F	Н
Me	\sim NH ₂	Me	F	н
Me	NH ₂	Me	F	н
Me	NH ₂ CHF ₂	Me	F	н
Me	CHF ₂ NH ₂	Ме	F · ·	н
Me	NH ₂ CHF ₂	Me	F	Н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	~~~NH	Me	F	Н
Me	A P	Me	F	Н
Me	~~N → N →	Me	F	Н
Me	N O OMe	Me	F	Н
Me	NH ₂	Me	F	н
Ме	N	Me	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	NH NN N	Me	F	н
Me	NO	Me	F	н
Ме	N N N N N N N N N N N N N N N N N N N	Me	F	н
Me	NS NS	Me	F	н
Me	CH₂OH		F	н
Me	CH₂OH	/	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	CH₂OH		F	н
Me	CH₂OH		F	Н
Ме	CH₂OH		F	н
Me	CH₂OH		F	н
Me	CH₂OH		F	н
Me	CH₂OH	CN	F	Н
Me	CH ₂ OH		F	н
Me	CH₂OH	\sim	F	Н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	CH₂OH	Me	CI	н
Me	CH₂OH	Me	Br	н
Me	CH ₂ OH	Me	CN	н
Me	CH ₂ OH	Me	Ме	н
Me	CH ₂ OH	Me	CF ₃	Н
Me	CH₂OH	Me	NO ₂	н
Me <u>.</u>	CH₂OH	. Me	F _.	ОН
Me	CH ₂ OH	Me	F	NH ₂
Me	CH ₂ OH	Me	F .	F
Me	CH ₂ OH	Me - 154 -	F	SH

$$R_4$$
 R_2
 R_3
 R_2
 R_3
 R_4
 R_5
 R_1
 R_1
 R_2
 R_3
 R_4
 R_5
 R_5
 R_7
 R_8
 R_9
 R_9

F

Me

Н

CH₂OH

R ₁	R ₂	R ₃	R ₄	R ₅
N N	CH₂OH	Me	F	н
N N	CH₂OH	Ме	F.	н
	CH₂OH	Me	F	н
N N NH	CH₂OH	Мө	F	н
N-N	CH₂OH	Ме	F	н
O	CH₂OH	Ме	F	н
O N	CH ₂ OH	Me	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
S N	CH₂OH	Me	F	н
	CH₂OH	Me	F	н
O	^{Me} CH₂OH	Me	F	н
N	CH₂OH	Me	F	н .
N	CH₂OH DMe	Me	F	н
Me	Me	Me	F	н
Me		Me	F	н
Me	OH	Me	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	NH ₂	Me	F	н
Ме	ОН	Me	F	н
Ме	NH ₂	Me	F	н
Ме	Ph NH ₂	Me	F	н
Me	OH	Me	F	н
Ме	\sim NH ₂	Me	F	н
Me	NH ₂	Me	F	н
Me	NH ₂ CHF ₂	Me	F	н
Mė	CHF ₂ NH ₂	Me	· F	н
Me	NH ₂ CHF ₂	Me	F	Н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	NH NH	Me	F	н
Me	→ H	Me	F	н
Me	√ NH O	Me	F	. н
Me	N OMe	Me	F	н
Me	N N N N	Me	F	н
Me		Me	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	N N	Me	F	Н
Me	NO	Me	F	н
Me	M N N N N N N N N N N N N N N N N N N N	Me	F	Н
Me	√ S N	Me	F	н
Me	CH₂OH		F	н
Me	CH₂OH	/	F	Н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	CH₂OH		F	н
Me	CH₂OH	\nearrow	F	н
Me	CH₂OH		F	н
Me	CH₂OH		F	н
Me	CH₂OH	\square	F	н
Me	CH ₂ OH	∕	F	Н
Me	CH₂OH		F	Н
Me	CH ₂ OH	\sim	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	CH₂OH	Me	CI	Н
Me	CH₂OH	Me	Br	H.
Me	CH₂OH	Me	CN	н
Ме	CH₂OH	Me	Me	н
Me	CH₂OH	Me	CF₃	Н
Ме	CH₂OH	Me	NO ₂	н
Me	CH₂OH	Me	F	ОН
Me	CH₂OH	Me	F	NH ₂
Me	CH₂OH	Ме	F	F
Me	CH₂OH	Me	F	SH

$$R_4$$
 R_3
 R_1
 R_2
 R_3
 R_4
 R_5
 R_1
 R_2
 R_3
 R_4
 R_5
 R_5
 R_1
 R_2
 R_3
 R_4
 R_5
 R_5
 R_7
 R_1
 R_2
 R_3
 R_4
 R_5
 R_5
 R_1
 R_2
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 R_5
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 R_4
 R_5
 R_5
 R_7
 R_7

Ме

F

Н

CH₂OH

R ₁	R ₂	R ₃	R ₄	R ₅
N N	CH₂OH	Me	F	н
N	CH ₂ OH	Мө	F	н
	CH₂OH	Me	F	н
N=NH	CH₂OH	Me	F	н
N-N	CH₂OH	Me	F	н
	CH₂OH	Me	F	Н
ON	CH₂OH	Me	F	н

R ₁	· R ₂	R ₃	R ₄	R ₅
s N	СН₂ОН	Me	F	Н
	СН₂ОН	Ме	F	н
OMe	CH ₂ OH	Me	F	н
N	СН₂ОН	Me	F	Н
OMe	СН₂ОН	Me	F	н
Me	Me	Me	F	н
Me		Me	F .	н
Me	ОН	Me	F	Н

R ₁	R_2	R ₃	R ₄	R ₅
Me	NH₂ Ph	Me	F	Н
Me	∕ ОН	Me	F	н
Ме	∕ NH₂	Me	F	н
Me	Ph NH ₂	Me	F	н
Me	OH	Me	F	Н
Me	\sim NH ₂	Me	F	Н
Me	NH ₂	Me	F	н
Me	NH ₂ CHF ₂	Me	F	н
Me	CHF ₂	Me	F ·	н
Me	NH ₂ CHF ₂	Me	F	н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	∕ NH	Me	F	Н
Ме	A P	Me	F	н
Me	~~N [™]	Me	F	н
Me	N OMe	Me	F	н
Me	N N N N N	Me	F	н
Me	N	Me	F	н

R ₁	R ₂	R ₃	R_4	R ₅
Me	N.N.	Me	F	Н
Me	NO	Me	F	н
Me	NH NH	Me	F	н
Ме	√√ _N S	Ме	F	н
Me	CH₂OH		F	н
Me	CH₂OH	/	F	Н

R ₁	R ₂	R ₃	R_4	R ₅
Me	CH₂OH	人	F	н
Me	CH₂OH		F	Н
Me	CH₂OH		F	Н
Me	CH₂OH		F	Н
Me	CH₂OH		F	н
Me	CH₂OH	CN	F	Н
Mė	CH₂OH		F	H
Me	CH ₂ OH		F	н

R ₁	R ₂	R ₃	R ₄	R ₅
Me	CH ₂ OH	Me	CI	н
Me	CH₂OH	Me	Br	н
Me	CH₂OH	Me	CN	н
Me	CH₂OH	Me	Me	н
Me	CH₂OH	Me	CF ₃	н
Me	CH₂OH	Me	NO ₂	н
Me	CH₂OH	Me	F .	ОН
Me	CH₂OH	Me	F	NH ₂
Me	CH₂OH	Me	F	F
Me	CH₂OH	Me - 170 -	F	SH

or a pharmaceutically acceptable salt or stereoisomer thereof.

7. A pharmaceutical composition that is comprised of a compound in accordance with Claim 1 and a pharmaceutically acceptable carrier.

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S. A method of treating or preventing cancer in a mammal in need of such treatment that is comprised of administering to said mammal a therapeutically effective amount of a compound of Claim 1.

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9. A method of treating cancer or preventing cancer in accordance with Claim 8 wherein the cancer is selected from cancers of the brain, genitourinary tract, lymphatic system, stomach, larynx and lung.

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10. A method of treating or preventing cancer in accordance with Claim 8 wherein the cancer is selected from histiocytic lymphoma, lung adenocarcinoma, small cell lung cancers, pancreatic cancer, gioblastomas and breast carcinoma.

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11. A process for making a pharmaceutical composition which comprises combining a compound of Claim 1 with a pharmaceutically acceptable carrier.

- 12. The composition of Claim 7 further comprising a second compound selected from:
 - 1) an estrogen receptor modulator,
 - 2) an androgen receptor modulator,
 - 3) a retinoid receptor modulator,
 - 4) a cytotoxic/cytostatic agent,
 - 5) an antiproliferative agent,
 - 6) a prenyl-protein transferase inhibitor,
 - 7) an HMG-CoA reductase inhibitor,
 - 8) an HIV protease inhibitor,
 - 9) a reverse transcriptase inhibitor,
 - 10) an angiogenesis inhibitor,
 - 11) a PPAR-γ agonist,
 - 12) a PPAR-δ agonists;

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13) an inhibitor of cell proliferation and survival signaling,

14) an agent that interfers with a cell cycle checkpoint, and

- 15) an apoptosis inducing agent.
- The composition of Claim 12, wherein the second compound is an
 angiogenesis inhibitor selected from the group consisting of a tyrosine kinase inhibitor, an inhibitor of epidermal-derived growth factor, an inhibitor of fibroblast-derived growth factor, an inhibitor of platelet derived growth factor, an MMP inhibitor, an integrin blocker, interferon-α, interleukin-12, pentosan polysulfate, a cyclooxygenase inhibitor, carboxyamidotriazole, combretastatin A-4, squalamine, 6-O-(chloroacetyl-carbonyl)-fumagillol, thalidomide,
 angiostatin, troponin-1, and an antibody to VEGF.
 - 14. The composition according to Claim 7 further comprising a proteosome inhibitor.
- 15. The composition according to Claim 7 further comprising a aurora kinase inhibitor.
 - 16. The composition according to Claim 7 further comprising a Raf kinase inhibitor.
 - 17. The composition according to Claim 7 further comprising a serine/threonine kinase inhibitor.

- 18. The composition according to Claim 7 further comprising an inhibitor of another mitotic kinesin which is not KSP.
 - 19. The composition of Claim 12, wherein the second compound is an estrogen receptor modulator selected from tamoxifen and raloxifene.
- 30 20. A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy.

A method of treating or preventing cancer that comprises administering a 21. therapeutically effective amount of a compound of Claim 1 in combination with a compound selected from: an estrogen receptor modulator, 1) 2) an androgen receptor modulator, 5 a retinoid receptor modulator, 3) a cytotoxic/cytostatic agent, 4) an antiproliferative agent, 5) a prenyl-protein transferase inhibitor, 6) an HMG-CoA reductase inhibitor, 10 7) an HIV protease inhibitor, 8) a reverse transcriptase inhibitor, 9) an angiogenesis inhibitor, 10) PPAR-y agonists, 11) PPAR-δ agonists, 12) 15 an inhibitor of inherent multidrug resistance, 13) 14) an anti-emetic agent, an agent useful in the treatment of anemia, 15) an agent useful in the treatment of neutropenia, 16) an immunologic-enhancing drug, 17) 20 an inhibitor of cell proliferation and survival signaling, 18) an agent that interfers with a cell cycle checkpoint, and 19) an apoptosis inducing agent. 20) A method of treating cancer that comprises administering a therapeutically 22. 25 effective amount of a compound of Claim 1 in combination with radiation therapy and a compound selected from: an estrogen receptor modulator, 1) 2) an androgen receptor modulator, a retinoid receptor modulator, 3) 30 a cytotoxic/cytostatic agent, 4) an antiproliferative agent, 5) a prenyl-protein transferase inhibitor, 6) an HMG-CoA reductase inhibitor, 7)

an HIV protease inhibitor,

8)

9) a reverse transcriptase inhibitor,

- 10) an angiogenesis inhibitor,
- 11) PPAR-γ agonists,
- 12) PPAR-δ agonists,

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- 13) an inhibitor of inherent multidrug resistance,
- 14) an anti-emetic agent,
- 15) an agent useful in the treatment of anemia,
- 16) an agent useful in the treatment of neutropenia,
- 17) an immunologic-enhancing drug,
- 18) an inhibitor of cell proliferation and survival signaling,
- 19) an agent that interfers with a cell cycle checkpoint, and
- 20) an apoptosis inducing agent.
- 23. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and paclitaxel or trastuzumab.
 - 24. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and a GPIIb/IIIa antagonist.
 - 25. The method of Claim 24 wherein the GPIIb/IIIa antagonist is tirofiban.
 - 26. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a COX-2 inhibitor.
 - 27. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a proteosome inhibitor.
- 28. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with an aurora kinase inhibitor.

29. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a Raf kinase inhibitor.

- 30. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a serine/threonine kinase inhibitor.
- 31. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with an inhibitor of a mitotic kinesin that is not KSP.
 - 32. A method of modulating mitotic spindle formation which comprises administering a therapeutically effective amount of a compound of Claim 1.
 - 33. A method of inhibiting the mitotic kinesin KSP which comprises administering a therapeutically effective amount of a compound of Claim 1.